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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,442	02/26/2004	Arthur Ashman	01527/100L635-US1	5006

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EXAMINER	
BERMAN, SUSAN W	
ART UNIT	**PAPER NUMBER**
1711	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,442	ASHMAN ET AL.	
	Examiner	Art Unit	
	/Susan W. Berman/	1711	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-34,94,95 and 100-103* is/are pending in the application.

4a) Of the above claim(s) *29-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-28,91,94,95 and 100-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07-06-2007 has been entered.

Response to Amendment

The rejection of claims as being unpatentable over Schacht '328 is withdrawn.

The rejection of claims over Anseth et al '599 in view of Schacht is maintained and has been rewritten in more detail as set forth herein below.

Response to Arguments

Applicant's arguments filed 7-06-2007 have been fully considered but they are not persuasive.

With respect to applicant's argument that a rational reason to combine an anhydride polymer and bone substitute is required to support an obviousness rejection, the reasons for the obviousness rejection were set forth in the rejection mailed 3-07-2007. Applicant's arguments rebuting the reasoning articulated in the 3-7-07 rejection that is relevant to the amended claims and the rewritten grounds of rejection over Anseth et al in view of Schacht set forth below are discussed herein.

Applicant argues that there is no suggestion in Anseth et al to combine a bone substitute with the prepolymers. This argument is unpersuasive because Anseth et al clearly teach adding bone regenerating molecules into the composition in orthopedic applications (column 8, lines 7-11). Applicant argues that there would been no reason to combine Anseth et al with Schacht since there was no evidence at the time of the invention that the Schacht polymers in combination with a bone substitute would work and test results (as discussed in the Declaration of Robert S. Langer) show that they do not work. This argument is not persuasive for the following reasons. The rejection is not based on substitution of the polymers taught by Schacht for those taught by Anseth et al. The rejection is based on employing the specified bone allografts taught by Schacht as the bone generating molecules in the compositions taught by Anseth et al.

The Declaration under 37 CFR 1.132 of Robert S. Langer that discusses the "Huys Study", the "Brooks" Study and the "Yukna Pilot Study" has been considered and found unpersuasive for the following reasons. Applicant relies upon the data in the Yukna Pilot Study to show that compositions comprising the prepolymer of the instant invention combined with a photoinitaitor and redox initiator provide good clinical osseaintegration compared with the compositions of the prior art.

Applicant argues that the polymers disclosed by Anseth et al in combination with calcium carbonate or Bioplant® HTR® or both were light cured in the Brooks study and shown to cause tissue necrosis. Applicant states that the initiating system did not contain both photoinitiator and redox initiator. The examiner has not found any disclosure of the kind of initiator(s) used in the Brooks study. The samples reported in the Brooks tests were light cured for five minutes and

produced inflammatory cells, necrotic bone with very few bone particles, plasma cells and giant cell reactions around the LC test material (shown in pictures 9-12 in the Declaration). Biopsies showed that methacrylic acid given off and not neutralized was probably responsible for the tissue necrosis. See pages 4-5 of the Declaration.

The data presented in US 2005/0052471 [CIP of the instant application] in Example 48 and discussed in the Declaration of Robert S. Langer has been considered. The data is considered to show that the materials employed did not cause significant inflammation, rejection, necrosis or foreign body reaction, as stated in Example 48. It is agreed that the results obtained are unexpected when considered in view of the prior art of record and the data reported in the Declaration of record. The data shows significantly improved results when the formulations employed include camphorquinone and ethyl 4-dimethylaminobenzoate and the porogens sucrose and gellaten in compositions F1 to F4, wherein F2 to F4 include Bone substitute Bioplant® HTR® and Formulations F2 and F3 also include calcium carbonate. Camphorquinone is disclosed as one of the suitable biocompatible photoinitiators (paragraph 0079 in US PREPUB '471 or Specification, page 21) and ethyl 4-dimethylaminobenzoate is disclosed as an amine accelerator in paragraph 0088 in US PREPUB '471 and as a reducing agent unsuitable for use with benzoyl peroxide on page 24 of the instant application. Formulations F1 to F3 contain 90% MCPP and 10% MSA prepolymers while formulation F4 contains 100% MSA prepolymer.

Although unexpected results are shown by comparative data, the instant claims are not considered to be commensurate in scope with the showing provided. There is no data provided wherein the prepolymer is MCPP alone. There is no data provided for bone substitutes other than a biocompatible microporous layered polymeric composite such as Bioplant® HTR®. There is no

data provided for photoinitiators that are not biocompatible. There is no data provided wherein the formulation contains an oxidizing agent. There is no data wherein the formulation contains one of the reducing agents disclosed in the instant application (see pages 23-24). The instant claims do not recite a porogen. It appears from the data that the presence of camphorquinone and ethyl 4-dimethylaminobenzoate is the factor that provides the unexpected results. However, the Examiner has not found any mention of the kinds of initiators present in samples L1 to L4 tested in the Brooks Study so it is not absolutely clear that it is the initiators that are the significant factors. The compositions L1 to l4 in the Brooks study were light cured and the formulations F1 to F4 in Example 28 of US PREPUB '471 were also light cured.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-28, 91, 94, 95 and 100-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anseth et al (5,902,599) in view of Schacht (6,933,328).

Anseth et al disclose biodegradable polymer networks obtained by polymerizing anhydride prepolymers including unsaturated crosslinking groups. Methacrylic acid dianhydrides of diacids such as sebacic acid or 1,3-bis(p-carboxyphenoxy)-hexane are disclosed. Anseth et al teach free radical photoinitiators for irradiation with light, thermal initiators and redox systems for crosslinking the prepolymers (column 5, line 61, to column 6, line 54). The prepolymers can be combined with fillers,

reinforcing materials and/or other materials needed for a particular implant (column 7, lines 53-58). Anseth et al teach incorporating bone regenerating molecules, seeding cells and/or tissue into the prepolymer prior to or after polymerization or applying them prior to or after formation of an implant at the implant site (column 8, lines 7-14). The difference from the instantly claimed invention are that Anseth et al do not specifically teach combining a photoinitiator and a redox sytem for curing or specifically mention bone substitutes such as alloplasts or allografts, etc., as the bone regenerating molecules.

Schacht discloses a composition comprising a crosslinkable prepolymer, such as a polyester, polyorthoester or polyacetal, and a mineral biologically active component for a bone implant or cement or a dental material. The crosslinkable multifunctional prepolymer in the second embodiment is crosslinkable and comprises a mineral biologically active component (column 3, line 60, to column 4, line 9). Schacht teaches formulating the crosslinkable prepolymers with a biologically active substance such as a bone morphogenetic protein or a transforming growth factor in order to solve problems of acidity, rate of pore formation and speed of degradability (column 4, lines 57, to column 5, line 3). Suitable polymer sequences for biodegradability may be poly-α-hydroxy acid or polyanhydride and the polymerizable groups are ethylenic or acetylenic unsaturations (column 6, lines 29-35, and column 7, line 62, to column 8, line 7). Polymerization initiators, including photoinitiators and/or redox initiators, and a dual curing system are taught in column 12, lines 30-65. Compositions containing bone substitutes, such as bone growth factors and fibroblast growth factors, are taught in column 10, lines 23-39. Porous polymeric particles are taught (column 10, line 61, to column 11, line 16). See Examples 12 and 21. See Example 15, wherein a hydroxy carbonic acid oligomer is reacted with methacrylic anhydride followed by reaction of the carbonic acid group to provide an N-hydroxy-succinimidyl end group that is coupled to an oligopeptide. Example 21 discloses a combination of bone allograft and curable composite wherein the curable composition is placed on top of an allograft filling.

It would have been obvious to one skilled in the art at the time of the invention to employ the bone allograft taught by Schacht as a material needed for orthopedic applications in combination with the crosslinkable anhydride prepolymers disclosed by Anseth et al. Anseth et al provide motivation by teaching that such materials can be added to the disclosed prepolymers. Schacht provides motivation by teaching that bone allograft can be combined with analogous compositions comprising analogous crosslinkable biodegradable prepolymers. The crosslinkable prepolymers comprising polymerizable end groups and a biodegradable region from a poly-α-hydroxy acid or a polyanhydride or mixtures thereof taught by Schacht for preparing a biodegradable implant are considered to be analogous to the biodegradable crosslinkable prepolymers for dental and orthopedic applications disclosed by Anseth (column 6, lines 29-35).

It would further have been obvious to one skilled in the art at the time of the invention to employ a photoinitiator and a redox system for crosslinking the compositions taught by Anseth et al in combination with Schacht. Anseth et al provide motivation by teaching that photoinitiators or thermal and redox systems are useful. Schacht provide motivation by teaching that a photoinitiator and redox system can be used in combination in analogous compositions. Thus, one skilled in the art at the time of the invention would have been motivated by a reasonable expectation of successfully provide a dual cure system for the compositions.

With respect to claims 25-28, the compositions taught by Anseth et al alone or in combination with Schacht would be expected to provide the recited biodegrading properties since the components taught by Anseth et al alone or in combination with Schacht correspond to the components set forth in claim 1 or claim 24.

Conclusion

Shastri et al (5,837,752) is cited as art of interest. Shastri et al disclose semi-interpenetrating polymer networks comprising a linear hydrophobic degradable polymer and monomers or macromers including an anhydride linkage. The compositions can include humoral factors to promote cell transplantation and engraftment (column 7, lines 3-19). The photocurable compositions disclosed include mixed methacrylic anhydrides of sebacic acid and of 1,3-bis(p-carboxyphenoxy)propane (Example 1). Shastri et al teach that the photo-cured wafers from example 1 do not produce necrosis of surrounding tissue upon implantation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Susan W. Berman/ whose telephone number is 571 272 1067. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Seidleck can be reached on 571 272 1078. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SB
7/21/2007

/Susan W Berman/
Primary Examiner
Art Unit 1711